Liza M. Walsh
Christine I. Gannon
Jessica K. Formichella
WALSH PIZZI O'REILLY FALANGA LLP
Three Gateway Center
100 Mulberry Street, 15th Floor
Newark, NJ 07102
(973) 757-1100

Of Counsel:
J.C. Rozendaal
Michael E. Joffre
Uma N. Everett
Christina Dashe
Tyler C. Liu
Paige E. Cloud
Ariana Randal
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Ave., NW, Suite 600
Washington, DC 20005
(202) 371-2600

Attorneys for Defendant Teva Pharmaceuticals USA, Inc.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ALKERMES, INC. and ALKERMES PHARMA IRELAND LIMITED, *Plaintiffs,* v. TEVA PHARMACEUTICALS USA, INC., *Defendant.*	Civil Action No. 20-12470 (MCA)(MAH) *Filed Electronically*

TEVA'S RESPONSIVE POST-TRIAL BRIEF

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

TABLE OF ABBREVIATIONS

'499 patent	U.S. Patent No. 7,919,499
Alkermes	Collectively, Plaintiffs Alkermes, Inc. and Alkermes Pharma Ireland Limited
Alkermes Br.	Alkermes's Opening Post-Trial Brief, filed on April 12, 2023 (D.I. 224)
ANDA	Abbreviated New Drug Application
ACOL	Alkermes's Proposed Conclusions of Law, filed on April 12, 2023 (D.I. 225)
APFF	Alkermes's Proposed Findings of Fact, filed on April 12, 2023 (D.I. 225)
AUC	Area Under the Curve
FDA	Food and Drug Administration
IPR	*Inter Partes* Review
Patent Office	United States Patent and Trademark Office
PLA	Polylactic Acid
PLGA	Polylactide-co-glycolide
PTAB	The Patent Trial and Appeal Board
RTCOL	Teva's Proposed Responsive Conclusions of Law, filed on May 19, 2023
RTPFF	Teva's Proposed Responsive Findings of Fact, filed on May 19, 2023
Teva	Defendant Teva Pharmaceuticals USA, Inc.
Teva Br.	Teva's Post-Trial Brief, filed on April 12, 2023 (D.I. 223)
TCOL	Teva's Proposed Conclusions of Law, filed on April 12, 2023 (D.I. 223-1)
TPFF	Teva's Proposed Findings of Fact, filed on April 12, 2023 (D.I. 223-1)

Alkermes would very much like to hold onto its fifteen-year-old monopoly for Vivitrol and delay generic competition for years. But the eighteen other patents that Alkermes previously listed in the FDA's Orange Book as covering Vivitrol have expired. TPFF517. And the evidence at trial showed that Alkermes's remaining patent—the asserted '499 patent—is invalid.

First, Alkermes's attempts to save its patent from indefiniteness rely on blithely ignoring the text of the patent claims. The claims require that individuals sick with addiction be given naltrexone and that doing so results in the claimed AUC ratio. But Alkermes asserts that the claims are definite because, once a particular kind of "comparative PK study" is performed for a given product in healthy people specifically over the intended time period of administration and the study shows that product, on average, achieves the claimed AUC ratio, then infringement occurs *whenever* it is administered to such sick people, regardless of what those sick people's AUC turns out to be. TPFF99–100; APFF251. None of that is in the patent.

Moreover, Alkermes's experts were asked how they would determine whether a given long-acting formulation would practice the AUC limitations of the claims under their own comparative PK-study requirements if the creator of that formulation changed its mind regarding the intended time period of administration. TPFF117. They could not agree how to do so. Teva Br. 16–17. If Alkermes's own experts cannot agree whether a formulation practices the claims under their own concocted criteria, then an accused infringer cannot either. The claims are indefinite.

Second, to save its patent from obviousness, Alkermes asks this Court to ignore statements in the prior art that refute its arguments. Comer's main conclusion was that a 384-mg dose of Depotrex was a "safe and effective" and an "important and exciting" treatment. Rather than address that conclusion, Alkermes focuses on two isolated disclosures in the prior art: (1) an

earlier report of injection-site induration for a 206-mg dose of Depotrex in Kranzler, and (2) Comer's observation that patients receiving 192 mg of Depotrex reported lower overall cravings for heroin as compared to those receiving 384 mg. RTPFF128–130, 137–140. Alkermes asserts (at Alkermes Br. 3, 20–23) that, based on these disclosures, a skilled artisan would not have selected the "important and exciting" 384-mg dose in Comer. RTPFF138. Again, that argument ignores what the prior art actually says. With respect to induration, Comer noted Kranzler's previous findings, decided to test a 384-mg dose anyway, and found no evidence of induration or any other "untoward side effects." RTPFF128, 132–133. Regarding cravings, far from concluding that the 384-mg dose was somehow ineffective, Comer instead found that both the 192-mg and the 384-mg doses worked and that the 384-mg dose worked longer than the 192-mg dose. RTPFF105, 138–139, 141–142.

Alkermes also (at 2, 14–15) asks this Court to focus on Dr. Ehrich's "novel hypothesis" that a higher exposure of long-acting naltrexone as compared to oral naltrexone was needed to fix the brain's "broken reward system"—and faults Teva (at 2) for failing to "cite prior art that taught Dr. Ehrich's theory to a POSA." But, critically, Dr. Ehrich's new-found theory is found nowhere in the '499 patent claims, specification, or file history. Teva Br. 8–10. And the law does not require that the prior art disclose an inventor's idiosyncratic motivations for arriving at an invention; instead, "*any* need or problem" can serve as a reason to arrive at the claimed combination. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 419–20 (2007) (emphasis added). Here, Alkermes *admits* (ACOL285) "there is no dispute" that a skilled artisan would have been motivated to address the problem of creating a safe and effective long-acting naltrexone treatment that improved patient compliance. That motivation would have led a skilled artisan to administer a long-acting, 384-mg naltrexone-PLGA formulation and achieve the claimed AUC

ratio. Therefore, the claims are invalid as obvious, regardless of what secret theories the inventor may have had. *Supra*; Teva Br. 17–38.

Finally, Alkermes attempts (at 24–26) to overcome obviousness by asserting that the claimed AUC ratio is not an inherent result of administering the claimed dose in a PLGA microsphere. Teva disputes the contention. If the Court nevertheless accepts it, however, then the patent is still invalid as it fails to provide a written description of the full scope of the claims. If something more is needed to achieve the claimed AUC besides simply administering the claimed dose within a PLGA microsphere, then the specification fails to show that Dr. Ehrich possessed whatever that something is. Teva Br. 39–40. In response, Alkermes asserts (at 38–39) that the claims are adequately described because a skilled artisan, reviewing the specification, would have found it "routine to adjust [a given] formulation as needed to achieve the claimed AUC." Alkermes gets the law wrong. Claims are not adequately described merely because a skilled artisan would have found them routine to achieve. *Rivera v. Int'l Trade Comm'n*, 857 F.3d 1315, 1322 (Fed. Cir. 2017); *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351–52 (Fed. Cir. 2010).

In sum, the Court should hold the asserted claims of the '499 patent are invalid.

I. Alkermes's own experts' testimony confirms the claims are invalid as indefinite.

Alkermes does not dispute the following: (a) determining whether a given long-acting formulation meets the recited three-times AUC ratio requires knowing the oral AUC (in the denominator) and the long-acting AUC (in the numerator); (b) the oral AUC varies greatly from study-to-study and patient-to-patient, and the long-acting AUC varies greatly depending on the length of time over which it is measured; (c) the ratio for a given formulation can thus change, and fall both inside and outside the scope of the claims, depending *solely* on how the numerator and denominator are selected; but (d) the '499 patent itself provides no AUC guidance at all, and

so does not explain how to arrive at those critical values. RTPFF58–61. Because a competitor trying to practice the invention or design around it would thus be unable to discern the bounds of the invention, the claims are invalid as indefinite. *See Nautilus, Inc. v. Biosig Inst., Inc.*, 572 U.S. 898, 901 (2014); *Forest Lab'ys, Inc. v. Teva Pharms. USA, Inc.*, 716 F. App'x 987, 994 (Fed. Cir. 2017) (compiling cases); RTCOL11. Ignoring this problem, Alkermes instead argues (at 37 n.23) that a skilled artisan would understand that the claims implicitly require a specific "comparative PK" study on healthy patients to "deal with" the admitted variance in the oral and long-acting AUCs. *See also* RTPFF60–61. But, as confirmed by Alkermes's own experts, this imagined comparative PK study explicitly contradicts the claim language. And, even on its own terms, it does not resolve indefiniteness.

A. The comparative PK study Drs. Peck and Little argue is required to determine the AUC directly contradicts the plain language of the claims.

Neither the claims nor the specification of the '499 patent mention, let alone require, any sort of comparative PK study. RTPFF68. Nevertheless, Alkermes asserts (at 36–37) that a "patent need not explicitly include information that is already well known in the art." And because (according to Alkermes) a skilled artisan would have known how to perform the recited AUC comparison with a comparative PK study, the claims have "an objective baseline" and are not indefinite. *Id.* (citing *Presidio Components, Inc. v. Am. Tech. Ceramics Corp*, 875 F.3d 1369, 1376 (Fed. Cir. 2017) and *Sonix Tech. Co., Ltd. v. Publ'ns Int'l, Ltd.*, 844 F.3d 1370, 1378–79 (Fed. Cir. 2017)). Alkermes is wrong on both the law and the facts.

As to the law, Alkermes's reliance on *Presidio* and *Sonix* is misplaced. In each, the patent specification provided explicit guidance to the skilled artisan regarding how to make the determination required by the claims, even though carrying out the determination involved some extrinsic knowledge. *See Presidio*, 875 F.3d at 1375–77 (where specification disclosed a single

method of measuring the recited "fringe-effect capacitance" but did not provide all the parameters for conducting such testing, the claims were not indefinite because a skilled artisan still would have understood how to perform the method); *Sonix*, 844 F.3d at 1378–79 (claims reciting "visually negligible" indicator not indefinite where the patent provided specific examples and other guidance allowing a skilled artisan to understand the term); *see also* RTCOL7–8. Here, by contrast, the '499 patent fails to contain *any* AUC or pharmacokinetic discussion, does not mention a comparative PK study, and says nothing about how such a study should be conducted. RTPFF67–68; TPFF56, 79–81, 584.

On the facts, Alkermes misrepresents Dr. Yaman's testimony when asserting (at 37) that the parties "agreed" that a skilled artisan would have understood that the AUC limitation requires a comparative PK study. RTPFF75–77. Dr. Yaman testified that a skilled artisan would know *how* one might conduct a comparative PK study to compare two drugs in general. RTPFF75–76. But the pertinent question is *whether* the claims (silently) require a comparative PK study in the first place. They do not. *See Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 (Fed. Cir. 2003) ("the analytical focus must begin and remain centered on the language of the claims themselves"). And Dr. Yaman never said otherwise. In fact, Dr. Yaman expressly testified to the opposite: such a comparative PK study finds no support in the patent, contradicts the plain language of the claims, and so cannot be used to show the claims are definite. RTPFF67, 77.

Consistent with Dr. Yaman's testimony, Alkermes's proposed PK study cannot be squared with the text of the claims. Drs. Peck and Little postulate a comparative PK study in a *group* of individuals who are *healthy*, but the claims recite treating "an individual in need of naltrexone"—i.e., an *individual* who is *sick*. RTPFF67, 77, 87; TPFF97–104. Tellingly, Dr. Little

recognizes that the first half of the claim (treating a sick individual by administering the long-acting formulation) is satisfied when the claimed formulation is given to a *sick individual.* TPFF99–101. But instead of asking whether that individual exhibits the required AUC ratio, Drs. Peck and Little both ignore that individual in the second half of the claim, turning instead to their postulated comparative PK study that is found nowhere in the patent.[1] TPFF97–99, 101–104; APFF251. That sudden shift in perspective highlights the error in Alkermes's reading of the claim. *See IGT v. Bally Gaming Int'l, Inc.*, 659 F.3d 1109, 1117 (Fed. Cir. 2011) ("claim language must be construed in the context of the claim in which it appears" and thus "refus[ing] to adopt" a construction that would "rewrite the claim" inconsistently with the surrounding context); *NeoMagic Corp. v. Trident Microsys., Inc.*, 287 F.3d 1062, 1075 (Fed. Cir. 2002) (same).

Alkermes's criticism (at 36–37) that Dr. Yaman "did not properly view the claims from the perspective of a POSA" by failing to apply a comparative PK study thus misses the mark. Dr. Yaman correctly testified that Alkermes's comparative PK study was unsupported by the patent and was contradicted by the plain language of the claims, and so did not allow for a skilled artisan to determine the scope of the claims. RTPFF67, 77. Alkermes's related criticism (at 37) that Dr. Yaman should not have used "cross-study comparison" is also flawed. A skilled artisan would understand that—unlike Alkermes's comparative PK study—such a cross-study comparison is one possible method to perform the recited AUC comparison that *is* at least consistent with the claim language and, as credibly explained by Dr. Yaman, shows the

[1] Alkermes asserts that it is Teva's position that the comparative PK study must be performed in a single sick patient. Alkermes Br. 37 n. 22. That is wrong. In fact, the whole problem is that there are multiple possible methods or parameters that could be used to perform the recited AUC comparison to get different results. Teva's point is that the comparison cannot be limited to *Alkermes's* specific, imagined comparative PK study because it is inconsistent with the patent.

indefiniteness of the claims. RTPFF87–88. Indeed, Dr. Ehrich himself used such a cross-study comparison in his declaration in order to calculate the AUC ratio between his long-acting formulation and the prior-art Tice formulation. RTPFF69, 88.

Lastly, Alkermes states that a skilled artisan would "see that Dr. Ehrich used such a [comparative PK study]" in his declaration submitted during prosecution, "which further confirms the reasonable clarity for a POSA." Alkermes Br. 37 n. 21. But the Federal Circuit has expressly warned against importing limitations from the file history into the claims, especially where (as here) they directly contradict the plain language of the claims.[2] *See Baxalta Inc. v. Genentech, Inc.*, 972 F.3d 1341, 1346 n.4, 1346–49 (Fed. Cir. 2020); RTCOL9; *see also* RTPFF67, 70, 77. Alkermes could have written claims to require a comparative PK study, but it did not. That drafting choice has legal consequences. "[T]he Court must judge the claims that were issued" and "those claims [are] indefinite." *Forest Lab'ys, Inc. v. Teva Pharms. USA, Inc.*, No. CV 14-1058-LPS, 2016 WL 54910, at *9 (D. Del. Jan. 5, 2016) (refusing to import pharmacokinetic study parameters used in an inventor declaration into the claims to save them from indefiniteness because there was "no proper basis" for limiting the claims to such a study and because the patentee could have specified such parameters in the claims but did not).

B. Drs. Peck and Little could not agree how to determine whether a given formulation falls inside or outside the scope of the claims.

Regardless of whether one uses a comparative PK study or some other method to determine the AUC ratio, the claims nevertheless suffer from the problem that they do not specify the time period over which to measure the long-acting AUC. TPFF109–122. Alkermes

[2] Further, as Teva previously explained, Dr. Ehrich's comparative AUC study does not even comply with Alkermes's new, imagined requirements for such a study because the long-acting AUC was not measured in the same group of individuals who received oral naltrexone. TPFF108; RTPFF69. So it cannot provide support for limiting the claims to avoid indefiniteness.

asserts (at 38) that, despite this silence, a skilled artisan would somehow know to "match" the timeframe for measuring the long-acting AUC to the *intended* treatment period. The *only* support Alkermes cites for this proposition from either the patent or the prosecution history is: (a) a single statement in the specification that "the formulation [of the invention] preferably releases naltrexone over a period of at least about one, two, three, or four weeks;" and (b) the fact that Dr. Ehrich's prosecution declaration described the treatment period for Vivitrol as 28 days and calculated the AUC of Vivitrol over a 28-day time period. APFF258–59 (citing DTX-001.008 (4:42–64) and PTX-52.001–02). Neither helps Alkermes.

Neither the single sentence Alkermes cites in the specification, nor any other part of the patent says anything about how to select the time period for measuring the claimed long-acting AUC, let alone tells a skilled artisan to "match" that time period for measuring to the time period of administration. DTX-001.0008 (4:42–64); RTPFF82 n. 5. And Dr. Ehrich's declaration actually underscores the claims' indefiniteness. First, Dr. Ehrich's declaration says nothing about "match[ing]" the time period for measuring the long-acting AUC to that of the time period for administration, nor does it discuss or explain how to practice the AUC limitations of the claims at all. RTPFF84. Instead, Dr. Ehrich stated in his declaration that the measured long-acting AUC was "$AUC_{0\text{-}28\ days}$"—i.e., Dr. Ehrich explicitly defined the time period for measurement rather than stating the intended treatment period should be matched to the period for measuring the long-acting AUC. *Id*. But there is no similar subscript or any other time period provided in any of the asserted claims. *Id*.

Further, Dr. Ehrich's declaration shows that attempting to match the timeframe for measuring the long-acting AUC with the intended treatment period does not actually resolve the lack of clarity. Dr. Ehrich calculated the AUC ratios for Vivitrol as well as the Tice formulation.

TPFF65, 122; RTPFF73, 83, 85. Yet, despite the fact that Tice and Vivitrol have effectively identical intended treatment periods—"once monthly" and "every 4 weeks or once a month," respectively—the time period Dr. Ehrich used for calculating the AUC of each was different: 32 days for Tice and 28 days for Vivitrol. RTPFF73, 83, 85. Thus, even if a skilled artisan were to attempt to match the time period for measuring the long-acting AUC to its treatment period, there would still be an array of potential time periods to choose from (e.g., for a "once monthly" treatment, the skilled artisan could feasibly measure AUC over the course of 28, 29, 30, 31, or even 32 days or more), and depending upon which one was chosen, the AUC ratio would change. TPFF93, 122; RTPFF73, 83, 85.

Alkermes further asserts that "the experts agreed at trial that a POSA would have been able to design a long-acting formulation to match" the intended treatment period, and so "the AUC would be calculated for that [] period." Alkermes Br. 38. This statement is false. Not even Alkermes's *own* experts agree this is how a skilled artisan would calculate the long-acting AUC.[3] Dr. Peck did *not* agree with Alkermes's proposition that a skilled artisan would automatically design a given long-acting formulation to match the intended treatment period. Instead, Dr. Peck admitted that the intent of the time period for measuring the long-acting AUC will change with the intent of the manufacturer: i.e., if the skilled artisan designed a long-acting product and then decided to change the intended treatment period for that product, then the product would stay the same but the AUC would be re-calculated using the new time period. TPFF114–117. Dr. Little disagreed with Dr. Peck's straightforward conclusion, and instead stated that a skilled artisan

[3] Nor does Dr. Yaman agree with this framework. While he agreed that a skilled artisan may have an intended time period for administration of a drug, that fact sheds no light on what time period a skilled artisan would understand the *claims* require for measuring the AUC. Dr. Yaman testified that the patent does not specify any time period for that measurement. RTPFF82; TPFF79, 81–82.

would necessarily design a formulation that would have its AUC measured over the intended treatment period; i.e., in Dr. Little's opinion, if a skilled artisan designed a long-acting product, but then made the decision to change the intended treatment period for that same product, then the artisan would necessarily need to "reformulate" an entirely new product whose AUC was necessarily measured over the time period he proposed. TPFF117. The contradictory testimony of Drs. Peck and Little thus shows that the claims fail "to provide sufficient notice" of their scope because they "depend[] 'on the unpredictable vagaries of any one person's opinion.'"[4] *Liberty Ammunition, Inc. v. United States*, 835 F.3d 1388, 1398 (Fed. Cir. 2016).

Finally, Alkermes argues (at 38) that "Teva's witnesses did not testify that Claim 2 was indefinite in this regard since Claim 2 is expressly limited to a treatment period of four weeks." Alkermes is wrong. Dr. Yaman provided extensive testimony showing that even specifying the treatment period does not provide clarity as to what time period to use to measure the long-acting AUC (nor does it provide any insight regarding what oral AUC value to use). So the mere fact that claim 2 specifies a four-week treatment period does not render the claim definite. RTPFF71–73, 82–85; TPFF118–122. In sum, Alkermes cannot overcome a finding of indefiniteness.

II. The evidence showed that a long-acting formulation of naltrexone and PLGA administered in a 384-mg dose was safe, effective, tolerable, and obvious.

Alkermes concedes that "there is no dispute that the problem facing a POSA at the time of the invention would have been a long-acting naltrexone treatment that was safe and effective

[4] Alkermes ignores that its experts cannot agree on the time period for measuring the long-acting AUC for the exact same product and instead asserts "the Patent Office never had any issues with the comparative AUC limitation in this regard." Alkermes Br. 38. The fact that claim terms were "considered by the Examiner, and ultimately allowed" does not mean they are definite because if this were the case, then "no approved patent term would be found to be indefinite." *TVnGO Ltd. (BVI) v. LG Electronics Inc.*, 861 F. App'x. 453, 458 (Fed. Cir. 2021); *Uni-Systems, LLC v. U.S. Tennis Ass'n Nat'l Tennis Ctr. Inc.*, 17-CV-147(KAM)(CLP), 2020 WL 3960841, *29, n.19 (E.D.N.Y. 2020).

and would improve patient compliance compared to oral naltrexone." APFF285. The evidence demonstrates that the prior art disclosed all the elements in the patent claims and that they could be combined with a reasonable expectation of success to solve that problem. Specifically, Comer and Nuwayser disclosed the 384-mg long-acting naltrexone-PLGA Depotrex treatment that was "safe and effective" with no "untoward side effects," that would improve patient compliance, and that inherently results in the recited AUC ratio. And Leavitt confirmed such a formulation would be effective in treating opioid and alcohol dependence. RTPFF128, 138, 145, 172, 186–207, 209–210, 244. The patent is therefore obvious, despite Alkermes's arguments to the contrary.

A. Comer's administration of two injections totaling 384-mg naltrexone teaches the administration step of the claims.

1. The claims are not limited to a single injection.

Alkermes first contends that, because the claims recite "the step of parenterally administering *a long-acting formulation*" comprising the recited dose of naltrexone, the dose must be given in a single injection. Thus, Alkermes argues (at 7–9) that Comer's use of two injections does not teach the administration step of the claims. But the wording of the claims disproves Alkermes's argument. Claim 1 simply recites "the step of parenterally administering a long-acting formulation comprising" the claimed amount of naltrexone, and the asserted dependent claims refer back to "the long acting formulation" of claim 1. DTX-001.0017. RTPFF152. None of the asserted claims recite or require that the administration step take place in a "single injection"; in fact, they do not recite the words "single" or "injection" at all. RTPFF153. The plain language of the claims thus simply requires that the formulation is parenterally administered in a "step" that delivers the claimed amount of naltrexone, regardless of whether that step involves one injection or multiple. RTPFF154–156.

Alkermes also states that the specification and file history somehow "confirm" that the claims are limited to a single injection because: (a) the working examples and Dr. Ehrich's declaration specifically describe the use of a "single injection"; and (b) the specification generally uses the term "a single [intramuscular] administration." Alkermes Br. 9. Yet neither the specification nor Dr. Ehrich's declaration require that the claimed invention be limited to a single injection, and instead (as confirmed by Dr. Westreich), a skilled artisan would have understood that the specification's use of the term "a single IM administration" meant "one or two or multiple injections to get up to the appropriate dosage amount." RTPFF163–166. Further, if anything, the patent and the prosecution history show that what matters for the claimed invention is that the administered dose achieve the key recited AUC ratio, regardless of how that dose is administered. RTPFF163, 165–166.

Alkermes cites two cases in an attempt to support its assertion that the claims' use of "*a* long-acting formulation" means that they are limited to a single injection. Alkermes Br. 8 (citing *Insituform Techs., Inc. v. Cat Contracting, Inc.*, 99 F.3d 1098, 1104–06 (Fed. Cir. 1996) and *Harari v. Lee*, 656 F.3d 1331, 1341 (Fed. Cir. 2011)). In both cases, the patent claims reciting "an" item or step could not be read to encompass more than one such item or step because such a reading would be inconsistent with the claimed invention as a whole. RTCOL19–20. That is not the case here. Alkermes has not and cannot point to anything showing that administering multiple injections during the same procedure would be inconsistent with the invention, either in achieving the claimed AUC ratio or in achieving a successful treatment.[5] RTPFF163–175. In

[5] Alkermes implies that the use of a single injection is important for improving patient compliance. *See, e.g.*, Alkermes Br. 23–34. Yet neither the patent nor the prosecution history say anything about the use of one injection versus multiple to achieve improved patient compliance. RTPFF169. Further, the evidence in this case shows there is no real difference between one injection or multiple with respect to patient compliance either. RTPFF170–175.

fact, Dr. Little's own testimony confirms that the use of multiple injections to deliver the claimed dose is not only consistent with the claimed invention but is covered by the asserted claims. Specifically, Dr. Little conceded that, in certain instances, Vivitrol's 380-mg dose is delivered in two injections during the same procedure, which—according to him—"seems like" it practices the asserted claims. TPFF370. Thus, *Insituform* and *Harari* are inapposite.

Alkermes also asserts that "Teva's witnesses" did not offer any opinions that the claims may cover multiple injections "based on the actual language of the patent claim" but simply took that understanding from counsel. Alkermes Br. 7. Not so. Dr. Westreich explicitly provided his "view as a person of skill in the art" that the claims were not limited to a single injection because the claims lacked an explicit limitation to a "single injection," so "one or two or multiple injections" could be used "to get up to the appropriate dosage amount." RTPFF155–156, 160. If anything, Alkermes's argument that Teva's witnesses took their understanding of the scope of the claims from counsel confirms they should not be limited to a single injection. Under Federal Circuit law, "a" is frequently held to mean "one or more," especially where (as here), the patentee fails to expressly limit the claims to the singular; Dr. Westreich accurately recounted his understanding of that law from counsel when opining that the claims' use of "*a* long-acting formulation" should not be limited to a single injection but instead encompasses one or more injections. RTPFF161–162; RTCOL16.

Ultimately, Alkermes's position regarding the single injection is litigation-inspired hindsight. When the Patent Office gave Alkermes and Dr. Ehrich the opportunity to explain how the claimed invention was different from the prior art, they said nothing regarding one injection versus multiple. RTPFF165. Now that Comer's disclosure of a long-acting naltrexone-PLGA injection administered in two injection totaling 384 mg has been substantively cited during this

litigation (when it was not during prosecution), Alkermes has decided that the difference between a single injection and two injections is a lynchpin for nonobviousness. RTPFF165; TPFF502–503. Alkermes should not be permitted now to rewrite its claims with a narrower scope to avoid the conclusion of obviousness. *See TI Grp. Auto. Sys. (N. Am.), Inc. v. VDO N. Am., LLC*, 375 F.3d 1126, 1139–40 (Fed. Cir. 2004) (reversing finding of nonobviousness because the district court had construed the claims too narrowly).

2. Regardless, it would have been obvious to administer Comer's 384-mg dose as a single injection.

Alkermes also incorrectly characterizes Teva's argument regarding the single injection issue to be that a skilled artisan would have "start[ed] with" the 192-mg dose in Comer and "reformulate[d] it into a single injection totaling 384 mg." Alkermes Br. 19. The claims are not limited to a single injection, so Comer's two-injection dose of 384 mg explicitly teaches the claimed administration step and does not need to be "reformulated."[6] However, should the claims be construed as limited to a single injection, *even then* Teva still has shown that a skilled artisan would have found it obvious to use a single injection to deliver the 384-mg dose. RTPFF177–185.

Alkermes attempts to resist this showing by stating that Teva's witnesses have provided only "conclusory and unsupported testimony" in support. Alkermes Br. 22. But this ignores Drs. Westreich's and Yaman's testimony that a skilled artisan would have been motivated by patients' discomfort with needles to reduce the number of injections. And it ignores Nuwayser's disclosure that Depotrex could be administered as a single injection, as well as Kranzler's

[6] In fact, the prosecution history of the '499 patent supports Teva's position that Comer's 384-mg dose need not be "reformulated" into a single dose to teach the administration step of the claims: in its decision to institute the IPR of the '499 patent, the PTAB found that Comer's disclosure of two injections totaling 384 mg taught this claimed step. TPFF369.

disclosure teaching a skilled artisan that the injection volume required for such an injection would not exceed safe limits set forth by the prior art. RTPFF179–180.

Alkermes also argues that a skilled artisan looking to improve patient compliance would have been dissuaded from creating a single injection in a 384-mg dose because of Kranzler's finding that a single injection of a 206-mg dose exhibited indurations. According to Alkermes, such indurations might cause patients not to return for subsequent treatments. Alkermes Br. 22–23 (citing Weiss Tr. 553:13–24). These assertions are unsupported by the evidence.

First, Dr. Weiss testified to the unsurprising proposition that, if side effects are too high, a patient would not want to take subsequent injections. RTPFF182. But his testimony fails to substantiate whether a 384-mg dose in a single injection *specifically* would cause an unacceptably elevated risk of side effects. *Id.* And, contrary to Alkermes's assertions, Kranzler did not say that a 384-mg single injection would exhibit unacceptably high injection side effects. Comer explicitly noted Kranzler's statements about indurations. But she did not consider them a problem and did not state that they suggested reducing the amount of naltrexone in the injection. Instead, Comer concluded that Kranzler showed that Depotrex injections were "safe and effective." RTPFF183. If anything, Kranzler shows that increasing the injection volume to accommodate Comer's full 384-mg dose in a single injection would not have been a concern, because, as discussed above, Kranzler's disclosures would have taught a skilled artisan that the volume required for a single injection of 384 mg would not have exceeded safe limits. RTPFF180. Further, Dr. Little confirmed that, even if a skilled artisan would have been concerned about issues with indurations that might stem from an increased amount of naltrexone in the injection, there were known techniques to deal with those issues; Dr. Westreich also confirmed that, although patients do not necessarily "like" injections, if they need it to be treated

for their dependencies, they will take an injection. TPFF488; RTPFF184 (Westreich Tr. 136:5–137:1).

Any purported issues with increased injection-site irritation stemming from administering Comer's 384 mg-dose in a single injection do not overcome the strong evidence of obviousness of a single injection. After all, getting stuck with a needle once is preferable to getting stuck with a needle twice. *See, e.g.*, *Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 739 (Fed. Cir. 2013) (although increasing the dose increased the chance of side effects, there was no evidence "the side effects would be serious enough to dissuade the development of [the claimed] product" and so potential for increased side effects did not render claimed invention nonobvious); *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1293 (Fed. Cir. 2013) (similar).[7]

Lastly, Alkermes points to the fact that BioTek "never claimed, made, or tested" a single injection of a 384 mg-dose of Depotrex as supposed evidence that a skilled artisan would not have found a single injection to be desirable. Alkermes Br. 3, 14, 22, 23, 29. That is simply irrelevant. In the § 103 obviousness inquiry, what matters is not whether a single entity or reference explicitly combined all the elements together into a single product or disclosure but rather what the prior art in combination fairly teaches to the skilled artisan. RTCOL59–60. Given the skilled artisan's motivation to reduce the number of injections and Nuwayser's teaching that the Depotrex formulation could feasibly be administered in a single injection, it would have been

[7] Alkermes's citation (at 23) of *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1298–99, 1306 (Fed. Cir. 2015), is inapposite. There, the claims were directed to the unexpected discovery that an increase in the concentration of BAK increased permeability into the cornea, and so prior art disclosing that BAK *decreased* permeability taught away from making the claimed invention. *Id.* In contrast, the asserted claims are not directed to any sort of unexpected solution to issues with indurations; indeed, the patent says nothing about indurations. RTPFF45, 119. Thus, even if a single injection of 384 mg would have increased induration issues, that is irrelevant to the obviousness of the asserted claims here. TCOL83 (teaching away must be "commensurate in scope with the ultimate claims at issue").

obvious to create a single injection containing Comer's 384 mg-dose. RTPFF177–185.

B. The prior art as a whole taught that multiple doses, including 384 mg, would be desirable for treatment, and it did not discourage selecting 384 mg.

Alkermes next argues that a skilled artisan would have been dissuaded from using Comer's "higher amount [of 384 mg naltrexone] as a treatment for dependence," given that Kranzler reported that the 206 mg-dose exhibited indurations and Comer reported that the 384-mg dose exhibited higher craving than a 192-mg dose. Alkermes Br. 20–24. Specifically, Alkermes asserts that Teva uses hindsight to ignore Kranzler's and Comer's teachings regarding indurations and cravings. Alkermes Br. 1, 19, 23. Yet Alkermes has "dr[awn] the wrong conclusion from the risk of [] falling prey to hindsight bias" by adopting "[r]igid preventative rules" that ignore the required "expansive and flexible approach to the obviousness question." *KSR*, 550 U.S. 398 at 401, 421–22.[8]

First, Alkermes would have this Court rigidly find that a skilled artisan would not select the 384-mg dose simply because Kranzler and Comer disclosed purported drawbacks for that dose and have this Court ignore the remaining statements and conclusions in those references demonstrating that 384 mg was desirable. Specifically, Alkermes spends pages discussing the purported issues of indurations and cravings reported in Kranzler and Comer but ignores Comer's overall conclusion that the 384-mg dose was safe and effective treatment. RTPFF128–

[8] Alkermes's overly rigid obviousness approach is underscored by its reliance (at 17) on *In re Kotzab*, 217 F.3d 1365, 1369–70 (Fed. Cir. 2000) and *In re Cyclobenzaprine*, 676 F.3d 1063, 1073 (Fed. Cir. 2012). *Kotzab* applied the "teaching, suggestion, or motivation" test for obviousness that the Supreme Court later overruled in *KSR* as being too narrow and formalistic, 550 U.S. at 418–19. And while Alkermes cites *Cyclobenzaprine* for the proposition that use of hindsight is a legal error, the court in that case actually held that use of hindsight is instead a factual issue, reviewed for "clear error." 676 F.3d at 1073. Alkermes's additional criticism that Drs. Yaman and Westreich occasionally said the invention "is obvious" rather than "would have been obvious" also shows its inappropriately rigid approach to obviousness. RTCOL25; RTPFF53.

130, 138–139. For example, *none* of the nearly 150 pages in Alkermes's post-trial submission mentions or addresses: (a) Comer's express statement that *both* the lower 192-mg dose and the higher 384-mg dose worked against the subjective effects of heroin; (b) Comer's data showing that the 384-mg dose maintained therapeutic blood plasma levels for longer than the 192-mg dose; and (c) Comer's overall conclusion that these results showed that Depotrex was "safe, effective, [and] long-lasting," making it an "important" and "exciting" once-a-month treatment option.[9] RTPFF138. Thus, far from Teva's witnesses ignoring "an express finding by the authors of the Comer paper" (Alkermes Br. 13, 20), it is Alkermes who ignores both *multiple* "express findings" of Comer and Comer's overall conclusions. RTPFF138–139.

Alkermes also would have this Court ignore Comer's teaching that any purported issues with indurations or cravings with the 384-mg dose were really no issues at all. With respect to indurations, Comer did not *decrease* the dose administered based on Kranzler, as Alkermes suggests. Alkermes Br. 3, 12. Instead, Comer explicitly noted Kranzler's induration findings, *increased* the highest tested dose anyway (from 206 mg to 384 mg), and ultimately found that neither indurations nor any other "untoward side effects" were "found in the present study."[10] RTPFF133. With respect to cravings, Comer never concludes that the 384-mg dose somehow did not work due to this purported issue or was not a desirable treatment. RTPFF139. Comer instead concludes the opposite: namely, that *both* doses of 192 mg and 384 mg of Depotrex worked

[9] The only positive finding regarding the 384-mg dose that Alkermes mentions is Comer's statement that 384 mg worked against the subjective effects of heroin for longer than the 192-mg dose. Alkermes Br. 13. But Alkermes wrongly implies that Comer otherwise found that 384 mg did not work, when her overall conclusion was precisely the opposite. RTPFF138.

[10] Alkermes incorrectly asserts (at 22 n.15) that Drs. Westreich and Yaman purportedly ignored the problem of indurations described in Kranzler. On the contrary, they credibly explained how Comer cited Kranzler, reported that Depotrex was safe and effective, and found Depotrex did not exhibit an increased amount of adverse effects despite increasing the dose from Kranzler. RTPFF134.

against the subjective effects of heroin, and "Depotrex" (and not just the 192-mg dose of Depotrex) was "safe, effective" and "exciting." RTPFF138–139.

Despite all this, Alkermes repeatedly points to Dr. Westreich's statement that the 192-mg dose of Depotrex "performed better" in the cravings metric than the 384-mg dose to assert that this would have dissuaded a skilled artisan from selecting the 384-mg dose. Alkermes Br. 13, 20–21. This does not help Alkermes's nonobviousness argument. The Federal Circuit has repeatedly held that, for obviousness, the prior art does *not* need to suggest that "the combination claimed by the patent [] is the preferred, or most desirable, combination," but instead it merely needs to "suggests the desirability of [that] particular combination." *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004); RTCOL40. Put another way, there is no requirement that an obvious choice be the "optimal" or "best" choice. *See Galderma Lab'ys, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 738–39 (Fed. Cir. 2013) (even though a lower concentration of drug would have been "optimal," and increasing the concentration would increase side effects, this would not have dissuaded a skilled artisan from selecting the claimed higher concentration because nothing suggested that such an increased concentration would be "unproductive" or that "side effects would be serious enough to dissuade the development of a 0.3% adapalene product"); *Par Pharm. Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1197–98 (Fed. Cir. 2014) ("[o]ur precedent, however, does not require that the motivation be the *best* option, only that it be a *suitable* option from which the prior art did not teach away").

Here, as discussed above, Comer provided a multitude of reasons that a skilled artisan would have found the 384 mg-dose of Depotrex to be overall desirable and suitable as a treatment option, and the prior art also did not discourage selecting this dose. TPFF227–234, 479–497; RTPFF128, 138–139, 141–142. Indeed, Alkermes admits that Comer taught that the

384-mg dose of Depotrex worked against the subjective effects of heroin more than the 192-mg dose, and Dr. Little admitted that Comer was not "discouraging people" but instead concluded that "a formulation of naltrexone [like Depotrex] that requires only once-a-month administration has important and exciting treatment implications." Alkermes Br. 13; TPFF493; RTPFF141–142. Thus, there can be no question that a skilled artisan would have, at the very least, viewed the 384-mg dose of Depotrex as a suitable treatment option for persons in need of naltrexone, which is all that the obviousness analysis requires. RTCOL40.

Finally, any issues of indurations and cravings ultimately do not provide persuasive evidence of nonobviousness here. The asserted claims and the '499 patent are not directed to solving or reducing indurations (indeed, Alkermes concedes that Vivitrol exhibits indurations and other injection-related side effects). TPFF489–491. Nor does the patent say anything about cravings, let alone claim a treatment of such issues; indeed, the only efficacy metrics set forth in the '499 patent relate to the reduction of inappropriate drinking behaviors. TPFF299, 497; RTPFF44, 214. Thus, neither indurations nor cravings can form the basis for an assertion of nonobviousness of the claims. TCOL80, 83.

C. Alkermes's assertion that the prior art did not disclose the same motivations as Dr. Ehrich's is legally irrelevant and contrary to the facts.

Alkermes repeatedly points to Dr. Ehrich's supposedly "novel" theory to assert that the prior art did not teach such a theory, which purportedly shows that the claimed invention was nonobvious. Alkermes Br. 2, 14–15, 21, 24. It does not.

1. Dr. Ehrich's theory is unsupported by the record and cannot be used to overcome the evidence that a skilled artisan would have been motivated to select Comer's 384-mg dose.

Dr. Ehrich's purportedly "novel hypothesis" or "theory"—that the "significantly higher exposure to naltrexone" exhibited by a 380-mg dose could fix the "broken reward system of

patients in need of naltrexone" is scarcely credible. Alkermes Br. 14–15. Dr. Ehrich admitted that his theory is not reported in the patent at all, and he did not explain this "different path" to the Patent Office during prosecution despite being given the opportunity to do so. TPFF301, 304–311; RTPFF248; Alkermes Br. 2. Instead, he simply pointed to achievement of an "unexpectedly high" AUC, while failing to mention he had already publicly disclosed such a high AUC years before. TPFF311–314.

Apart from Dr. Ehrich's self-serving trial testimony, there is no evidence that he had any such novel hypothesis at the time he applied for the patent. On the contrary, far from showing that the 380-mg dose worked but the 190-mg dose did not (as Dr. Ehrich testified, TPFF286), the patent states that "good to excellent results" were achieved with *both* the 190 mg *and* the 380-mg dose. The patent even has claims on the 190-mg dose. TPFF303.

2. The prior art, including Alkermes's own prior art, confirm a skilled artisan's motivations.

Even if Dr. Ehrich did have a "novel hypothesis" regarding achievement of the claimed AUC ratio to fix the brain, it would be irrelevant to the obviousness inquiry. A skilled artisan need not be motivated by the same hypotheses or issues as the inventor; instead, a skilled artisan may be motivated by "any need or problem" known in the art. *KSR*, 550 U.S. at 419–420; *see also Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1197 (Fed. Cir. 2014) ("we are not limited to the same motivation that may have motivated the inventors" and so it was appropriate to "look[] to motivations beyond" the inventor's achievement of a recited inherent property).

Here, Alkermes agrees that a skilled artisan would have been motivated to create "a long-acting naltrexone treatment that was safe and effective and would improve patient compliance compared to oral naltrexone." ACOL285; Alkermes Br. 10, 18. The prior art disclosed that such a formulation should target naltrexone blood plasma levels of greater than about 1–2 ng/ml for at

least about a month in order to be a successful once-a-month treatment that improved compliance. TPFF218–226; RTPFF101–107. A skilled artisan would have thus understood that Comer's 384-mg dose achieved each of these goals and would have further understood that the Nuwayser patent described the PLGA microspheres used in that formulation. TPFF227–238; RTPFF105–107, 127, 172, 244. That Teva did not cite prior art explicitly disclosing Dr. Ehrich's theory or the targeting of the claimed AUC ratio is irrelevant because Teva provided evidence that a skilled artisan would have understood that Comer and Nuwayser disclosed a treatment that had already solved the known need in the art in the same way as the claimed invention. *Novo Nordisk A/S v. Becton Dickinson & Co.*, 304 F.3d 1216, 1219 (Fed. Cir. 2002); *Geo. M. Martin Co. v. All. Machine Sys. Int'l LLC*, 618 F.3d 1294, 1305 (Fed. Cir. 2010) (where others independently arrived at the same invention as the patentee shows that the claimed invention "was the product only of ordinary [] skill").

In response, Alkermes contends that a skilled artisan would not have been motivated to target naltrexone plasma levels of greater than about 1–2 ng/ml and, instead, would have specifically targeted an AUC that "match[ed]" the FDA-approved 50 mg/day oral naltrexone. Alkermes Br. 18, 20 n. 12. These assertions have no basis in fact.

First, Alkermes asserts that it was only the "old Verebey reference" from the 1970s that stated therapeutic plasma levels were greater than about 1–2 ng/ml; and by 2001, Comer had rejected that study and instead found that "negligible" plasma levels were sufficient. Alkermes Br. 20, n.12; APFF114. Not so. Teva has cited a wealth of prior-art spanning from the 1980s all the way to Alkermes's own 2003 Bartus prior-art reference (which cites Verebey) that say that therapeutic plasma levels are greater than about 1–2 ng/ml. TPFF220–225; RTPFF101–103. Further, Comer never "reject[ed] Verebey" as Alkermes asserts. If anything, Comer taught that

"elevat[ed]" naltrexone plasma levels above at least 1–2 ng/ml would be desirable. RTPFF104–107.

Second, Alkermes asserts (at 21) that a skilled artisan would not have wanted to increase the level of exposure over oral naltrexone three-fold, as it could increase naltrexone's known side effects. That argument is directly contradicted by the fact that skilled artisans—including Dr. Weiss—understood that oral doses of naltrexone *higher* than 50 mg/day might provide greater efficacy than the FDA-approved dose and would not be toxic. RTPFF113. It is also contradicted by the fact that any concerns over side effects from use of heightened amounts of long-acting naltrexone doses were not ultimately "borne out" in the prior art. RTPFF121–135.

Alkermes's citation to Leavitt and Comer as stating that the 50 mg/day oral dose was "optimal" or "standard" also does not help. Alkermes Br. 18, 28. The considerations for a long-acting naltrexone formulation are significantly different than those for oral naltrexone. Therefore, the optimal or standard *oral* dose does not dictate the dose or exposure for a *long-acting* formulation. RTPFF114. For example, despite Comer explaining that the "standard" oral dose was 50 mg/day, Dr. Comer said nothing about matching exposure to that dose. Instead, she approvingly reported that Depotrex resulted in "elevat[ed]" plasma levels and provided data showing that the 384-mg dose of Depotrex achieved AUC values about three times greater than oral naltrexone without demonstrating significant side effects. TPFF475; RTPFF105, 113, 116.

In fact, Alkermes cites only a single prior art reference to support its assertion that a skilled artisan would have intended to develop a long-acting naltrexone product with a "comparable" exposure to 50 mg/day oral naltrexone: the Tice reference. Alkermes Br. 18 n.10, 21 n.13, 28. Yet Tice merely notes that its specific long-acting naltrexone formulation achieved comparable exposure to oral naltrexone. RTPFF108–112. It does not suggest that a skilled

artisan must match the exposure of long-acting naltrexone to that of oral naltrexone. Nor does it advise deviating from the widely accepted and widely reported therapeutic naltrexone blood plasma levels of greater than about 1–2 ng/ml when creating a long-acting naltrexone formulation. RTPFF110.

Finally, Alkermes's assertions that a skilled artisan would match the exposure of oral naltrexone are directly contradicted by Alkermes's own prior statements.[11] For example, as discussed above, Alkermes's 2003 Bartus prior-art reference explicitly states that "one approach" to improve patient compliance over oral naltrexone "would be to develop an injectable formulation that would maintain plasma levels within the therapeutic range" of ">2 ng/mL" "for approximately 1 month" in order to "assure[]" compliance. TPFF250–252. Similarly, Dr. Ehrich authored a public presentation in 2000 stating that "adequate blood levels" of naltrexone included those "greater than 2 nanograms per milliliter for a sufficient duration, e.g., one month," and doses of long-acting naltrexone up to 900 mg revealed no serious or adverse events. TPFF254, 470. Alkermes's contrary assertions in this litigation should be given the weight they deserve.

D. The prior art exhibited the claimed AUC ratio.

Confronted with Federal Circuit case law squarely holding that an otherwise obvious method of using a formulation cannot "become patentable merely by testing and claiming an inherent [blood concentration] property," Teva Br. 3, Alkermes asserts that the claimed AUC

[11] To be clear, Teva is *not* arguing that the manner in which Dr. Ehrich came up with the claimed invention is what renders it obvious. Instead, Teva points to Alkermes's own publicly presented work simply to demonstrate that its new, litigation-driven arguments contradict its prior public statements. *See Taylor v. Republic Servs., Inc.*, 968 F. Supp. 2d. 768, 775 (E.D. Va. 2013) (appropriate to disregard testimony of any witness "when satisfied that the witness is not telling the truth, or the testimony is inherently improbable due to inaccuracy, uncertainty, interest, or bias").

ratio is *not* an inherent property of the claimed naltrexone-in-PLGA formulation. Alkermes Br. 24–26.

The problem for Alkermes is that *all* of the naltrexone-PLGA formulations in this case that otherwise fall within the claims—Comer, Vivitrol, and Teva's ANDA product—exhibit the claimed AUC ratio. RTPFF193, 207; *Hospira Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1329–30 (Fed. Cir. 2020) ("the work of the inventor or the patentee can be used as the evidence of inherency"); *Par Pharm., Inc. v. TWi Pharms., Inc.*, 120 F. Supp. 3d 468, 474–75 (D. Md. 2015) (examples in the asserted patent, the patent owner's product, and the accused ANDA product supported finding of inherency). Put another way, giving any of these naltrexone-PLGA formulations to patients will automatically result in the claimed AUC ratio (assuming the ratio is measured as Dr. Ehrich did in his declaration).

Seeking to avoid the conclusion of inherency, Alkermes cites (at 24) *Millennium Pharms., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017), and *Endo Pharms. Solutions, Inc. v. Custopharm Inc.*, 894 F.3d 1374, 1381 (Fed. Cir. 2018). But those cases are readily distinguishable, as neither involved claims reciting the blood plasma properties stemming from administration of a formulation that was already disclosed in the prior art. *See* RTCOL65–66. Alkermes's reliance on the Tice reference (Alkermes Br. 25 n. 17) for the proposition that the dose of naltrexone does not necessarily determine the AUC is also irrelevant because Tice does not disclose a long-acting formulation with PLGA. Tice discusses a different polymer, called PLA. Therefore, it has zero bearing on whether administering a long-acting *PLGA* formulation will inherently result in the recited AUC ratio. RTPFF206.

Alkermes (at 25–26) additionally faults Dr. Yaman for using a cross-study comparison of "unrelated studies" rather than a single comparative PK study to show that Comer inherently

discloses the claimed AUC ratio. However, as explained above, the comparative PK study that Alkermes would have the claims require directly contradicts their plain language. *Supra* Section I. Moreover, Dr. Yaman performed the calculation using the exact same oral AUC values and the exact same time period for measuring the long-acting AUC as used by Dr. Ehrich. Performing the calculation exactly as Dr. Ehrich did revealed that Comer's 384-mg dose achieved the claimed AUC ratio.[12] RTPFF199. Alkermes relied on Dr. Ehrich's calculations to obtain its patent; it cannot now require more simply because it is trying to avoid a finding of inherency.

Finally, Alkermes points to Dr. Yaman's testimony that varying the ratio of glycolic acid and lactic acid in the PLGA polymer can change the AUC. Alkermes Br. 24–25. Again, irrelevant. All of the naltrexone-PLGA formulations in this case, including the prior-art Comer formulation, resulted in the claimed AUC limitation. RTPFF193. The fact that some other PLGA theoretically might yield some other value makes no difference, because the prior art here actually yielded the claimed value. Moreover, to the extent that there is some magic in the ratio of glycolic acid to lactic acid so that the AUC value is not inherent, then Alkermes has never explained what that is. In that case, the claims are invalid for lacking written description. *See infra* Section V.

E. A skilled artisan would have had a reasonable expectation that the 384-mg dose of Depotrex could be successfully used in a method of treating addiction.

Finally, Alkermes asserts (at 26–29) that the claims are not obvious because a skilled

[12] Dr. Yaman also confirmed that, contrary to Alkermes's assertions (at 26), a skilled artisan "most certainly" would have looked to Comer's published blood plasma data and (using Dr. Ehrich's AUC methodology) that data would have revealed the three times AUC property. RTPFF88, 200; TCOL56. Dr. Ehrich similarly compared blood plasma data reported by different studies to evaluate AUC ratios, further demonstrating that a skilled artisan would have understood that a cross-study comparison is an appropriate methodology for evaluating comparative AUC ratios, including for Comer's AUC ratio as compared to oral naltrexone. RTPFF69, 88.

artisan would not have expected Comer's 384-mg dose of Depotrex to be successful. Alkermes focuses its argument regarding the purported lack of a reasonable expectation of success on the facts that: (a) Comer was a small study that showed increased cravings for the 384-mg dose, it could not "rule out" issues with indurations, and did not actually treat any patients; and (b) BioTek purportedly did not engage in "[f]uture studies" to establish efficacy after Comer or ultimately obtain FDA approval for Depotrex.[13] Alkermes Br. 12–13, 21 n. 14, 24, 26–29. These arguments are all flawed.

To start, Alkermes mischaracterizes both Comer's teachings and BioTek's actions regarding Depotrex. As discussed above, Comer explicitly taught a skilled artisan that Depotrex, including in a 384-mg dose, would be "safe and effective," have "no untoward side effects," and would thus be an "important and exciting" once-a-month treatment option. *Supra* § II.B. A skilled artisan seeing these unequivocal teachings would expect that the 384-mg dose of Depotrex would be successful. Further, while Dr. Comer disclosed that "future studies" would occur, she did not say that they were needed to somehow initially establish efficacy. On the contrary, she explicitly stated that Depotrex had already been shown to be safe and effective. RTPFF144. And contrary to Alkermes's assertions, these future studies not only *did* occur (as Comer was a Phase I study and Mr. Kerrigan confirmed Depotrex made it to Phase II trials), but Depotrex's clinical studies showed it was a clinical success and merely encountered economic issues, rather than any technical failures, in obtaining FDA approval. RTPFF5, 146, 263.

Alkermes effectively asks this Court to require that the prior art provide a conclusive

[13] Alkermes also cites Comer's and Leavitt's discussion that the "standard" or "optimal" dose of oral naltrexone was 50 mg/day and would have caused a skilled artisan to not "reasonably expect success" with a long-acting dose achieving three times the exposure of that oral dose. Alkermes Br. 28. That is incorrect for the same reasons as discussed above in Section II.C.2, *supra*.

proof of efficacy for Comer's 384-mg dose and that Depotrex needed to obtain FDA approval to be considered. RTCOL50. Yet the Federal Circuit has squarely rejected both requirements for establishing a reasonable expectation of success. *See, e.g.*, *Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.*, 903 F.3d 1310, 1333–34 (Fed. Cir. 2018) (because "[t]his court has long rejected a requirement of 'conclusive proof of efficacy,'" rejecting any requirement that there must have been "perfectly designed" clinical trials establishing efficacy); *Cubist Pharms., Inc. v. Hospira, Inc.*, 805 F.3d 1112, 1122–25 (Fed. Cir. 2015) (finding reasonable expectation of success despite lack of prior clinical trials where the prior art disclosed "extensive laboratory research" that predicted the success of the claimed dosing regimen); *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013) ("[t]here is no requirement that one of ordinary skill have a reasonable expectation of success in developing [the FDA-approved product]"; instead, one "need only have a reasonable expectation of success of developing the claimed invention"); TCOL64; RTCOL50–51. All that needs to be shown here is that a skilled artisan would reasonably expect that the 384-mg dose could successfully be used in an attempt to care for those with dependencies. *Id.* The evidence overwhelmingly shows the prior art provided exactly that. RTPFF209–217.

In sum, Alkermes's assertion (at 27) that Drs. Yaman and Westreich provided only "conclusory" testimony regarding reasonable expectation of success cannot be squared with their hundreds of pages of testimony providing concrete evidence of such an expectation, which Alkermes simply ignores.[14] RTPFF251; RTCOL62–63.

[14] Alkermes's cited law—*Insite Vision Inc. v. Sandoz, Inc.*, 783 F.3d 853, 859–61 (Fed. Cir. 2015), and *Amgen Inc. v. F. Hoffmann-La Roche Ltd.*, 580 F.3d 1340, 1363 (Fed. Cir. 2009)—is thus inapposite since the evidence in those cases failed to show that the skilled artisan would have had any sort of reasonable expectation that the claimed combination would work.

III. The dependent claims fail to save the '499 patent from a finding of obviousness.

Alkermes contends that asserted dependent claims 2, 10, and 13 contain additional requirements beyond those in asserted claims 1 and 5 that also would not have been obvious to a skilled artisan.[15] Alkermes Br. 29–32. Alkermes is wrong.

A. Alkermes fails to show there is something special about the specific concentration of naltrexone recited in claim 13.

Alkermes states that Nuwayser does not disclose the specific 35% concentration of naltrexone recited in claim 13 because: (i) its working examples regarding naltrexone specifically used concentrations greater than 50%; and (ii) Teva did not show any motivation for a skilled artisan to reduce that concentration to 35% as claimed. Alkermes Br. 14, 29–30. These arguments violate two longstanding Federal Circuit doctrines.

First, Alkermes's focus on Nuwayser's working examples to the exclusion of Nuwayser's teachings as a whole is error. A prior-art patent "must be considered for all that it teaches to those of ordinary skill in the art, not just the embodiments disclosed therein." *In re Arora*, 369 F. App'x 120, 122 (Fed. Cir. 2010). Dr. Yaman confirmed that Nuwayser's specification teaches that active ingredients, including naltrexone, can be formulated into PLGA microspheres in the manner disclosed and that naltrexone specifically can be present in such microspheres in the range from 0.1 to 80%. RTPFF233. Dr. Yaman further confirmed that a skilled artisan would have understood there was "nothing all that special" about the specifically claimed 35% concentration within Nuwayser's range and "would know exactly what to do" to get to that 35% from Nuwayser's disclosure. RTPFF233.

[15] Dependent claim 5 merely specifies that the dose of naltrexone in 380 mg and the AUC is "about 3.3" times that of oral naltrexone, Alkermes Br. 6, and so Comer's and Nuwayser's disclosures of a 384-mg dose and achievement of about 3.3 times AUC render claim 5 obvious for the same reasons as claim 1. *Supra*.

These teachings lead to Alkermes's second problem. Where, as here, the prior art discloses a range for some aspect of an invention—even a broad range—claims directed to points within that range (here, the recited 35% concentration) are presumed obvious because it is not inventive to discover optimum or workable amounts within a previously disclosed range using routine experimentation. *In re Aller*, 220 F.2d 454, 456 (C.C.P.A. 1955); *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018); TCOL71–75; RTCOL74, 75. Once Teva demonstrated that the claim falls within a range disclosed in the prior art, the burden shifts to Alkermes to show that the claimed concentration is patentably different from the other concentrations in the prior-art range, i.e., that it is special, critical, or achieved unexpected results, or the prior art taught away from the claimed 35%. *Id.* Alkermes's attempts to make *Teva* shoulder the burden to explain why a skilled artisan would have selected the claimed 35% concentration gets the law backwards.[16]

Because Alkermes does not even mention the Federal Circuit's framework, it does not attempt to apply it. Alkermes thus makes *no* argument that the recited 35% concentration is somehow special or critical or provides unexpected results. RTPFF235–238. Alkermes suggests in its proposed findings of fact that a skilled artisan would have been discouraged from using 35% naltrexone due to concerns over side effects, but Alkermes provided no evidence supporting this assertion (if anything, the evidence instead shows a skilled artisan would not have any such concerns). RTPFF239–242. Further, the patent confirms that the 35% concentration is not critical. The "key" and "unexpected" property achieved by the claims is the three-times-AUC result. Yet *every* asserted claim recites achievement of that AUC, even those allowing the use of

[16] Alkermes's reliance on *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984), is inapposite because it did not deal with the overlapping range framework at issue in this case.

any concentration of naltrexone. The specification also explicitly envisions using anywhere from 30% to 75% naltrexone in the claimed formulations. RTPFF237–238. There is nothing special about 35%.

B. Claims 2 and 10 do not add anything nonobvious.

Claims 2 and 10—specifying administering the long-acting formulation once every four weeks for 24 weeks (claim 2) and treating alcohol dependence (claim 10)—do not add anything nonobvious to claims 1 and 5, as evidenced by the fact that Alkermes simply rehashes the same arguments as before. Alkermes Br. 30–32.

Repeated administration recited in claim 2 would have been obvious. Alkermes again asserts that Comer's and Kranzler's teachings regarding indurations and cravings would have dissuaded a skilled artisan from selecting Comer's 384-mg dose, including specifically from using that dose for repeated, monthly administration. Alkermes Br. 31–33. As explained above, the prior art taught that these issues were not real issues at all. So they do not support any assertion that a skilled artisan would avoid repeating Comer's 384-mg dose. *Supra*. Alkermes also asserts (again) that because Dr. Comer and BioTek did not themselves perform the claimed steps (here, repeat administration of the 384-mg dose over multiple months) this provides evidence of nonobviousness. As before, Alkermes misapprehends the law, which looks at what the prior art fairly suggests, not what the authors actually did. TCOL54–55; RTCOL59–60. Here, Comer explicitly taught that the 384-mg dose would be an effective "'once-a-month' treatment," and (consistent with Leavitt's teachings that long-term naltrexone therapy would be preferred) discloses that naltrexone can be administered over the course of a year. RTPFF228–230; TPFF385–389. Comer and Leavitt expressly teach the long-term therapy of claim 2.

Treating alcohol dependence would have been obvious. For claim 10, Alkermes similarly repackages its earlier arguments. Alkermes asserts that a skilled artisan would not have

used Comer's 384-mg dose to treat alcohol addiction as in claim 10 specifically because: (a) Comer excluded patients dependent on alcohol; and (b) Kranzler and BioTek's own actions would have confirmed that the effective dose for alcohol dependent patients was 206 mg or lower. Alkermes Br. 30–32. First, as previously explained, what matters is what the prior art taught: here, Comer expressly taught (consistent with Leavitt) that Depotrex was "safe and effective" for alcohol dependency. RTPFF209, 220–225. Additionally, as also previously explained, the mere fact that Kranzler may have taught that doses of 206 mg or lower would be effective for alcohol dependence does not matter for obviousness because Comer taught a skilled artisan that the 384-mg dose *also* would be effective for alcohol dependence, exactly as claimed. RTPFF223–224; RCOL40.

IV. Alkermes's arguments regarding secondary considerations are insufficient to overcome the strong *prima facie* case of obviousness.

As described above, Comer and Nuwayser described the long-acting Depotrex naltrexone treatment that practiced every element of the claimed method, years before the patent. *Supra*. Since Alkermes was not the first to come up with a long-acting naltrexone-PLGA treatment administered in the claimed dose, Alkermes's secondary considerations evidence cannot tip the scales to nonobviousness. *See Nalpropion Pharms, Inc. v. Actavis Lab'ys FL, Inc.*, 934 F.3d 1344, 1355–56 (Fed. Cir. 2019) (secondary considerations evidence could not overcome obviousness as "[t]he inescapable, real-world fact here is that people of skill in the art *did combine*" the prior art in the manner claimed); *Zup, LLC v. Nash Mfg., Inc.*, 896 F.3d 1365, 1374–75 (Fed. Cir. 2018) (differences between prior-art and the claims were minimal, so secondary considerations did not support nonobviousness). Further, Alkermes's secondary considerations evidence is weak.

No Nexus. Alkermes argues that it is entitled to a presumption of nexus "[b]ecause the

FDA-approved use of 'Vivitrol is an embodiment of the '499 patent'"—i.e., "there is a relationship between the claimed subject matter of the patent and the particular objective indicia." Alkermes Br. 33. Alkermes misstates the law. The mere fact that Vivitrol embodies the claims only meets half the test to trigger the presumption. To establish a presumption of nexus, the patentee must show that the "product embodies the claimed features, *and* is coextensive with them." *Fox Factory, Inc. v. SRAM, LLC*, 944 F.3d 1366, 1373 (Fed. Cir. 2019) (emphasis added). Yet not a single Alkermes witness provided testimony or any other evidence that the patent claims are co-extensive with Vivitrol. Drs. Peck and Weiss did not even address nexus at all, and Dr. Little testified only that Vivitrol embodies the claims. TPFF521–523; RTPFF254.

Further, Alkermes concedes that Vivitrol contains its proprietary Medisorb PLGA delivery technology prepared pursuant to its unasserted patents. Therefore, Vivitrol is plainly *not* co-extensive with the asserted claims, which do not recite or require any specific PLGA technology at all. TPFF507–520; RTPFF255–257. Alkermes attempts to dismiss this fatal flaw by arguing that Medisorb is simply "an 'inactive ingredient' which by itself would provide no clinical benefit to patients." Alkermes Br. 33. Yet Alkermes ignores its own admissions that Medisorb provides various clinical benefits such as once-a-month administration and a gradual release of naltrexone at a controlled rate. TPFF510–511; RTPFF257. Moreover, it was on the basis of its patents on Medisorb that Alkermes achieved *fifteen years* of a monopoly on Vivitrol. It is more than a little cynical for Alkermes to simultaneously use Medisorb to keep patients from buying a cheaper, generic version of Vivitrol for fifteen years and now to claim that Medisorb provides no clinical benefit to patients.

Thus, Alkermes has not established any presumption of nexus. Moreover, even if Alkermes enjoyed such a presumption (it does not), it is easily rebutted by the evidence showing

that any beneficial features of Vivitrol were already known and disclosed in the prior art and are not tied to any purportedly unique property. RTPFF258. Thus, as a matter of law, there is no nexus between Vivitrol and Alkermes's secondary considerations evidence, and so they cannot be used to demonstrate that the claims are not obvious. TCOL91–92.

No long-felt unmet need or failure of others. Alkermes asserts there was an unmet need for an improved treatment for alcohol and opioid dependencies that was safe, effective, and had sufficient tolerability to increase compliance over oral naltrexone. Alkermes Br. 11, 33–34. Alkermes can make that assertion only by ignoring the fact that BioTek already achieved such an improved treatment (Depotrex) years before the patent. RTPFF260. Alkermes points out that Vivitrol achieved FDA approval, whereas Depotrex did not. Alkermes Br. 16, 34. True enough. But lack of FDA-approval is only probative of nonobviousness where it indicates a need for, or a failure to achieve, a safe and effective treatment. RTCOL96–98. That is not the case here, as Depotrex was a "successful," and "safe and effective" treatment that simply failed to achieve FDA approval because of financial, rather than technical, issues. RTPFF5, 262–263.[17]

No relevant industry skepticism. Alkermes's evidence of purported skepticism focuses on *oral* naltrexone. Alkermes Br. 34 (citing oral naltrexone's purported lack of efficacy, the fact that patients would "quit" oral naltrexone, and the fact that the medical community purportedly

[17] Alkermes's cited law is inapposite. *See* Alkermes Br. 34 (citing *Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 998 (Fed. Cir. 2009); *In re Cyclobenzaprine*, 676 F.3d at 1082–83). In *Procter & Gamble*, the defendant tried to argue there was no failure of others or long-felt unmet need given that another drug received FDA approval before the patented drug, but the other drug was not produced until 10 years after the filing date of the patent. 566 F.3d at 998. Here, Depotrex was the subject of multiple publications years *before* the patent. And in *Cyclobenzaprine*, the claims covered an extended-release drug where the prior art disclosed test results for such an extended-release drug but explicitly found it was not therapeutically effective. 676 F.3d at 1081–83. Here, the prior art explicitly reported Depotrex *was* effective.

did not initially accept Vivitrol after launch due to skepticism surrounding oral naltrexone); RTPFF266. Such evidence regarding *oral* naltrexone cannot support any legally relevant industry skepticism regarding the feasibility of *a long-acting naltrexone formulation* like the one claimed. *See Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 885–886 (Fed. Cir. 1998) (relevant consideration is whether there was skepticism in the art of following the inventor's path); *see also* RTCOL101, 105. And far from the industry expressing skepticism regarding long-acting naltrexone formulations, the prior art is instead replete with teachings that such formulations would improve the patient compliance issues that caused the very oral naltrexone-related skepticism Alkermes cites. RTPFF267–268. Alkermes also did not substantiate its assertion that the medical community did not initially accept Vivitrol's utility but later realized its benefits over oral naltrexone. Alkermes Br. 34–35. Instead, the evidence shows that: (a) Alkermes simply ran into initial marketing and access issues for Vivitrol unrelated to relevant industry skepticism; and (b) far from the medical community accepting Vivitrol over oral naltrexone, even as of 2018, Vivitrol had a significantly smaller number of total prescriptions as compared to oral naltrexone. RPTFF269–272. There is thus no relevant factually supported industry skepticism showing nonobviousness.

No unexpected results. At trial, Dr. Ehrich confirmed that he told the Patent Office that Vivitrol exhibited an "unexpectedly high" AUC as compared to what people "outside the company" would have expected, and it was this AUC result that caused the claims' allowance. TPFF311, 498–499. Perhaps in view of Dr. Ehrich's later concession at trial that this unexpectedly high AUC was actually publicly disclosed to people outside the company as early as 2000, Alkermes has now changed its unexpected results story. TPFF500; RTPFF274–275.

Alkermes now asserts that in view of "what was being reported about both oral and

experimental long-acting formulation[s] (e.g., BioTek's formulations)," a skilled artisan would not have expected that Vivitrol would be "safe, effective, and tolerable." Alkermes Br. 35. But any comparison between Vivitrol and oral naltrexone formulations is irrelevant to the obviousness inquiry because oral naltrexone is not the closest prior art, which is instead Comer and Nuwayser's disclosure of the 384-mg dose of Depotrex. RTPFF276; TCOL94. Alkermes's further statement that a skilled artisan would not have expected an approximately 380-mg dose of naltrexone to be safe, effective, and tolerable is also directly contradicted by the closest prior art stating that the 384-mg Depotrex dose was "safe and effective" and had "no untoward side effects." RTPFF47, 128, 138, 279. That a long-acting formulation administered in a 380-mg dose, like Vivitrol, was safe, effective, and tolerable would have been entirely expected to a skilled artisan. *Compare Adapt Pharma Operations Ltd., v. Teva Pharms. USA, Inc.,* 25 F.4th 1354, 1373 (Fed. Cir. 2022) (where the claimed formulation purportedly exhibited an unexpected increase in bioavailability, there were no unexpected results where a POSA would have expected that using the claimed components in the claimed way would result in such an increase); *with Millennium Pharms.*, 862 F.3d at 1367–68 (finding unexpected results where the prior art failed to disclose the unexpectedly beneficial results of claimed invention).

No relevant copying. Alkermes's reliance on Teva's purported copying of Vivitrol rather than BioTek's formulations is unavailing, given that this is a Hatch-Waxman case. Alkermes Br. 35. Because BioTek did not receive FDA approval for Depotrex (for economic rather than clinical reasons), Teva could not have taken advantage of the significant economic incentives provided by the Hatch-Waxman Amendments had it chosen to base its long-acting naltrexone product on Depotrex rather than FDA-approved Vivitrol. RTPFF283; RTCOL108. It is because of these real-world *regulatory* and *economic* considerations, rather than technical considerations,

that the Federal Circuit has repeatedly held that a generic's decision to seek approval for a copy of the brand drug is not relevant to nonobviousness of patents covering the brand drug. *Bayer Healthcare Pharms., Inc. v. Watson Pharms., Inc.*, 713 F.3d 1369, 1377 (Fed. Cir. 2013); *Adapt Pharma*, 25 F.4th at 1374; *see also* RTCOL109–111 (explaining that Alkermes's cited law is either outside the unique Hatch-Waxman context or predates this controlling Federal Circuit law).

Alkermes's evidence regarding secondary considerations is thus irrelevant and insufficient to overcome the clear and convincing proof that the patent claims are obvious.

V. If the claimed AUC ratio is not inherent as Alkermes asserts, the claims lack written description.

The asserted claims cover the use of *any* PLGA polymer to achieve the recited AUC properties. TPFF578–579. To the extent that achievement of the claimed AUC ratio is *not* an inherent property of naltrexone-in-PLGA formulations, the patent fails to describe how to achieve the claimed AUC property with any other PLGA polymer besides Medisorb. The specification thus does not provide adequate written description for the full scope of the claims. TPFF575–591; RTPFF287–294. Put simply, Alkermes cannot require that the prior art show possession of an invention that the patent fails to show Dr. Ehrich possessed.

Alkermes points to the fact that the specification describes "examples of other suitable extended release technologies" besides Medisorb (such as Prolease and Resomer) and also provides various disclosures within the incorporated Wright patent and working Example 1 regarding preferred characteristics of PLGA polymers. Alkermes Br. 5, 39. Yet Alkermes concedes that there is no data in the specification regarding how to achieve the recited AUC ratio at all. TPFF590. Therefore, it does not disclose how any "other suitable" technologies could be used to achieve that property. RTPFF288–290; TPFF584. Further, Wright and Example 1 relate

only to Medisorb and so similarly do not provide written description support for the many dozens of PLGA polymers covered by the claims that could be used to achieve the AUC.[18] RTPFF289–292.

In response, Alkermes asserts only that Dr. Yaman admitted a skilled artisan would have found it "routine to adjust the formulation as needed to achieve the claimed AUC." Alkermes Br. 39. That fact is legally irrelevant to the written description inquiry here. "[T]he written description inquiry looks to 'the four corners of the specification' to discern the extent to which the inventor(s) had possession of the invention as broadly claimed" and so while "[t]he knowledge of ordinary artisans may be used to inform what is actually in the specification, [it may not be used] to teach limitations that are not in the specification, even if those limitations would be rendered obvious by the disclosure in the specification." *Rivera*, 857 F.3d at 1322. Thus, even if a skilled artisan would have found it routine or obvious from the specification to create formulations achieving the recited AUC ratio, that sheds no light on whether a skilled artisan would be able to discern that *Dr. Ehrich possessed* the full scope of PLGA polymers that would achieve that property, which it does not. TPFF591; RTPFF291–294. The claims thus lack written description.

CONCLUSION

The Court should hold that the asserted claims of the '499 patent are invalid.

Dated: May 19, 2023

Respectfully submitted,

Of counsel:
J.C. Rozendaal

By: */s/ Liza M. Walsh*
Liza M. Walsh

[18] *Vanda Pharms., Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1136 (Fed. Cir 2018), cited by Alkermes is thus inapposite because the specification in that case provided examples supporting the full scope of the claims, rather than one single embodiment. *Id.* (claims reciting a reduction in dose if someone was a poor metabolizer had adequate description where the specification gave *multiple* examples of how to adjust doses downward).

Michael E. Joffre
Uma Everett
Christina Dashe
Tyler Liu
Paige Cloud
Ariana Randal
Sterne, Kessler, Goldstein & Fox P.L.L.C.
1100 New York Ave., NW
Washington, DC 20005
(202) 371-2600

Christine I. Gannon
Jessica K. Formichella
Walsh Pizzi O'Reilly Falanga LLP
Three Gateway Center
100 Mulberry Street, 15th Floor
Newark, New Jersey 07102
(973) 757-1100

Attorneys for Defendants
Teva Pharmaceuticals USA, Inc.